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L with rhtB	7

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L3

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<u>Set Name</u> side by side	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u> result set
<i>DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ</i>			
<u>L3</u>	L with rhtB	7	<u>L3</u>
<u>L2</u>	L1 with (homoserine resistance)	0	<u>L2</u>
<u>L1</u>	amino acid production	356	<u>L1</u>

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Search Results - Record(s) 1 through 7 of 7 returned.

☐ 1. Document ID: US 20020102670 A1

L3: Entry 1 of 7

File: PGPB

Aug 1, 2002

PGPUB-DOCUMENT-NUMBER: 20020102670

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020102670 A1

TITLE: DNA coding for protein which confers on bacterium Escherichia coli resistance to L-homoserine, and method for producing L-amino acids

PUBLICATION-DATE: August 1, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Livshits, Vitaly Arkadievich	Moscow		RU	
Zakataeva, Natalya Pavlovna	Moscow		RU	
Aleoshin, Vladimir Venyamiyovich	Moscow		RU	
Balareova, Alla Valentinovna	Moscow		RU	
Tokhmakova, Irina Lvovna	Moscow		RU	

US-CL-CURRENT: [435/116](#); [435/193](#); [435/252.3](#); [435/69.1](#); [536/23.2](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw Desc	Image
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☐ 2. Document ID: US 20020058314 A1

L3: Entry 2 of 7

File: PGPB

May 16, 2002

PGPUB-DOCUMENT-NUMBER: 20020058314

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020058314 A1

TITLE: DNA coding for protein which confers on bacterium escherichia coli resistance to L-homoserine, and method for producing L-amino acids

PUBLICATION-DATE: May 16, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Livshits, Vitaly Arkadievich	Moscow		RU	
Zakataeva, Natalya Pavlovna	Moscow		RU	
Aleoshin, Vladimir Venyamiyovich	Moscow		RU	
Balareova, Alla Valentinovna	Moscow		RU	
Tokhmakova, Irina Lvovna	Moscow		RU	

US-CL-CURRENT: [435/106](#); [435/193](#); [435/252.3](#); [435/69.1](#); [536/23.2](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWC	Draw Desc	Image
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☐ 3. Document ID: US 20020055151 A1

L3: Entry 3 of 7

File: PGPB

May 9, 2002

PGPUB-DOCUMENT-NUMBER: 20020055151

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020055151 A1

TITLE: Fermentation process for the preparation of L-threonine

PUBLICATION-DATE: May 9, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hermann, Thomas	Bielefeld		DE	
Rieping, Mechthild	Bielefeld		DE	

US-CL-CURRENT: 435/106; 435/252.33

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWC	Draw Desc	Image
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☐ 4. Document ID: US 6303348 B1

L3: Entry 4 of 7

File: USPT

Oct 16, 2001

US-PAT-NO: 6303348

DOCUMENT-IDENTIFIER: US 6303348 B1

TITLE: DNA coding for protein which confers on bacterium escherichia coli resistance to L-homoserine and method for producing L-amino acids

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWC	Draw Desc	Image
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☐ 5. Document ID: EP 1013765 A1

L3: Entry 5 of 7

File: EPAB

Jun 28, 2000

PUB-NO: EP001013765A1

DOCUMENT-IDENTIFIER: EP 1013765 A1

TITLE: Gene and method for producing L-amino acids

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWC	Draw Desc	Image
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☐ 6. Document ID: EP 994190 A2

L3: Entry 6 of 7

File: EPAB

Apr 19, 2000

PUB-NO: EP000994190A2

DOCUMENT-IDENTIFIER: EP 994190 A2

TITLE: DNA conferring L-homoserine resistance to bacteria, and its use

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Draw Desc	Image
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☐ 7. Document ID: US 20020102670 A1 EP 994190 A2 AU 9947550 A JP 2000116390 A SK 9901408 A3 CA 2284850 A1 ZA 9906042 A CN 1254014 A RU 2144564 C1 BR 9904955 A KR 2000029006 A MX 9909343 A1 US 6303348 B1 US 20020058314 A1

L3: Entry 7 of 7

File: DWPI

Aug 1, 2002

DERWENT-ACC-NO: 2000-273530

DERWENT-WEEK: 200253

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TITLE: Novel RhtB protein, useful for generation of L-homoserine resistance in Escherichia bacteria and large-scale production of e.g. L-homoserine and L-alanine

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Draw Desc	Image
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BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO,
CABA,
CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB,
DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 14:16:56 ON
27 SEP 2002

SEA (AMINO ACID PRODU?)

74 FILE AGRICOLA
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1558 FILE CAPLUS
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97 FILE CIN
8 FILE CONFSCI
1 FILE CROPB
5 FILE CROPU
4 FILE DDFB
7 FILE DDFU
1260 FILE DGENE
4 FILE DRUGB
18 FILE DRUGU
335 FILE EMBASE
158 FILE ESBIODBASE
5 FILE FEDRIP
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808 FILE USPATFULL

9 FILE USPAT2
2 FILE YETU
235 FILE WPIDS
235 FILE WPINDEX
L1 QUE (AMINO ACID PRODU?)

FILE 'CAPLUS, BIOSIS, BIOTECHDS, MEDLINE, EMBASE, SCISEARCH' ENTERED AT
14:22:14 ON 27 SEP 2002

L2 4 S L1 (S) L-HOMOSERINE
L3 3 DUP REM L2 (1 DUPLICATE REMOVED)
L4 1 S L1 (S) RHTB
L5 27 S RHTB
L6 16 DUP REM L5 (11 DUPLICATES REMOVED)

=> d 16 ibib ab 1-16

L6 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:276181 CAPLUS

DOCUMENT NUMBER: 136:305142

TITLE: Fermentation process for the preparation of L-amino acids using recombinant strains of the family Enterobacteriaceae

INVENTOR(S): Rieping, Mechthild; Bastuck, Christine; Hermann, Thomas; Thierbach, Georg

PATENT ASSIGNEE(S): Degussa A.-G., Germany

SOURCE: PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002029080	A2	20020411	WO 2001-EP10209	20010905
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10130192	A1	20020411	DE 2001-10130192	20010622
AU 2001093795	A5	20020415	AU 2001-93795	20010905
PRIORITY APPLN. INFO.:			DE 2000-10048605 A	20000930
			DE 2000-10055516 A	20001109
			DE 2001-10130192 A	20010622
			WO 2001-EP10209 W	20010905

AB The invention relates to a fermn. process for the prepn. of L-amino acids,

esp. L-threonine and provides genetically modified microorganisms of the family Enterobacteriaceae enhanced to produce the desired product. The process consists of the following steps are carried out: fermn. of the microorganisms of the family Enterobacteriaceae producing the desired L-amino acid, in which microorganisms at least the pckA gene and/or the open reading frames yjfa and ytfP are individually or jointly attenuated and enrichment of the L-amino acid in the medium or in the bacterial cells, and isolation of the L-amino acid. Thus, Escherichia coli strain K12 MG442.DELTA.pckA, contg. an inactivated pckA gene, produced 3.7 g/L L-threonine compared to 1.5 g/L from the unmutated strain.

L6 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:72263 CAPLUS

DOCUMENT NUMBER: 136:133691

TITLE: Recombinant Enterobacteriaceae overexpressing malate:quinone oxidoreductase gene mqo and their use in threonine production

INVENTOR(S): Rieping, Mechthild; Thierbach, Georg; Van Der Rest, Michel Eduard; Molenaar, Douwe

PATENT ASSIGNEE(S): Degussa AG, Germany

SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002006459	A1	20020124	WO 2001-EP5548	20010516
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
DE 10103874	A1	20020131	DE 2001-10103874	20010130
US 2002127678	A1	20020912	US 2001-801042	20010308
PRIORITY APPLN. INFO.:			DE 2000-10034833 A	20000718
			DE 2001-10103874 A	20010130
			US 2000-229329P P	20000901

AB The invention provides a process for the fermentative prepn. of L-threonine using Enterobacteriaceae which in particular already produce L-threonine and in which the nucleotide sequence(s) which code(s) for the mgo gene are enhanced, in particular over-expressed. Thus, the mgo gene of Escherichia coli was overexpressed in E. coli. The transformant produced 2-fold more threonine than did the parent bacteria.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L6 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:349112 CAPLUS

DOCUMENT NUMBER: 136:354249

TITLE: Fermentative production of L-amino acids with poxB mutants of Enterobacteriaceae

INVENTOR(S): Thierbach, Georg; Rieping, Mechthild

PATENT ASSIGNEE(S): Degussa A.-G., Germany

SOURCE: Ger. Offen., 22 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10112107	A1	20020508	DE 2001-10112107	20010314
WO 2002036797	A2	20020510	WO 2001-EP11228	20010928
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2002015910	A5	20020515	AU 2002-15910	20010928
PRIORITY APPLN. INFO.:			DE 2000-10054748 IA	20001104
			US 2000-248210P P	20001115
			DE 2001-10112107 A	20010314
			US 2001-283612P P	20010416

AB The invention concerns a procedure for the fermentative prodn. of L-amino acids, in particular L-threonine, in which the poxB gene of an L-amino acid-producing microorganism of the family Enterobacteriaceae is inactivated and the resulting mutant is cultured to produce the L-amino acid. The mutant may addnl. overexpress another gene which enhances L-amino acid biosynthesis. Thus, a deletion mutation was introduced into the poxB gene of L-threonine-producing E. coli MG442. This mutant was further transformed with expression plasmids for the gdhA or rhtC genes. L-Threonine prodn. with the rhtC gene-expressing, .DELTA.poxB strain was increased approx. 2.6-fold relative to the parent strain.

L6 ANSWER 4 OF 16 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-10679 BIOTECHDS

TITLE: Fermentative preparation of L-threonine by employing Enterobacteriaceae bacteria in which nucleotide sequence(s) that code(s) for malate:quinone oxidoreductase (mgo) gene

are

enhanced, particularly over-expressed;
involving fermentation and vector-plasmid
pMW218mgo-mediated malate, quinone oxidoreductase gene
transfer and expression in Escherichia coli

AUTHOR: RIEPING M; THIERBACH G; VAN DER REST M E; MOLENAAR D

PATENT ASSIGNEE: DEGUSSA AG

PATENT INFO: WO 2002006459 24 Jan 2002

APPLICATION INFO: WO 2000-EP5548 18 Jul 2000

PRIORITY INFO: DE 2001-1003874 30 Jan 2001

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-217000 [27]

AB DERWENT ABSTRACT: NOVELTY - Fermentative preparation (M1) of L-threonine involves employing Enterobacteriaceae bacteria, in particular those

which

already produce L-threonine and in which the nucleotide sequence(s)

which

code(s) for the malate:quinone oxidoreductase (mgo) gene are enhanced,

in

particular over-expressed. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a polypeptide (I) from Enterobacteriaceae with malate:quinone oxidoreductase (Mgo) activity (E.C.1.1.99.16) is a polypeptide (a) having a fully defined sequence of 529 amino acids (S2) as given in the specification, (b) having an amino acid sequence which is at least 70% (preferably 95%) identical to (S2), (c) including deletion, insertion or exchange of one or more amino

acids,

(d) including N- or C-terminal lengthening by one or more amino acids, where the total length of the polypeptides according to (b)-(d) is 514-544 (preferably, 519-539), and in preferred form is 524-534 (preferably, 527-531) amino acid radicals; (2) a polynucleotide (II)

from

Enterobacteriaceae which codes for (I) is a DNA (a) that contains a nucleotide sequence corresponding to nucleobases 7-1593 of a fully defined sequence of 1720 nucleotides (S1) as given in specification, (b) that is degenerate with respect to (S1) due to degeneracy of genetic code, (c) that is a mutant with respect to (S1), containing sense mutations of neutral function, or (d) which is at least 70% (preferably, 95%) identical to (a) or (b), or (e) which is a polynucleotide that hybridizes with any one of the above mentioned sequences; (3) a plasmid pMW218mgo which contains the mgo gene of Escherichia coli; (4) a Mgo protein from Enterobacteriaceae with a N-terminal amino acid sequence of LNAVSM or AVSMAAK; and (5) a L-threonine-producing strain (III) of the genus Escherichia with the genetic and phenotypic features of the strain B-3996kurDELTAtdh/pVIC40, pMW218mgo. BIOTECHNOLOGY - Preferred Polynucleotide: (II) is a DNA which is capable for replication and codes for a polypeptide having a sequence of (S2). Preferred Method: (M1) most preferably involves carrying out the following steps: (i) fermentation

of

microorganisms of the family Enterobacteriaceae in which at least the mgo gene is enhanced (overexpressed), optionally in combination with further genes, and (ii) concentration of the L-threonine in the medium or in the cells of the microorganisms Enterobacteriaceae, and (iii) isolating a L-threonine. In (M1), the Enterobacteriaceae bacteria (preferably, E.coli, or a bacteria of the genus Serratia), comprise further genes which are enhanced in addition to the mgo gene, e.g. (i) genes of the thrABC operon which code for aspartate kinase, homoserine dehydrogenase, homoserine kinase and threonine synthase, (ii) pyc gene coding for pyruvate carboxylase, (iii) pps gene coding for phosphoenol pyruvate synthase, (iv) ppc gene coding for phosphoenol pyruvate carboxylase, (v) genes pntA and pntB coding for transhydrogenase, (vi) rhtB gene which imparts homoserine resistance, (vii) gdhA gene coding for glutamate dehydrogenase, or (viii) rhtC gene imparting threonine resistance, that are enhanced at the same time. Preferably, bacteria (i) in which the metabolic pathways reducing formation of L-threonine are at least partly eliminated, and/or (b) which are transformed with a plasmid vector (pMW218mgo) that carries the nucleotide sequence coding for mgo gene, are employed. Optionally, along with the mgo gene expression, isopropyl beta-D-thiogalactoside expression is induced. The bacteria preferably comprises nucleotide sequence coding for Mgo protein (i) with the N-terminal amino acid sequence MAAKAK corresponding to (S2), (ii) with the N-terminal amino acid sequence of LNAVSM, or (iii) with the N-terminal amino acid sequence of AVSMAAK. USE - For preparing L-threonine by fermentation (claimed). The method is useful for preparing L-threonine and L-isoleucine. ADVANTAGE - The process provides improved fermentative preparation of L-threonine. EXAMPLE - Preparation of L-threonine with the strain B-3996kurDELTAtdh/pVIC40, pMW218mgo was carried out as follows. Preparation of the strain B-3996kurDELTAtdh/pVIC40 pMW218mgo involves culturing the L-threonine-producing Escherichia coli strain B-3996, described in US5175107-A in antibiotic-free complete medium for approximately ten generations to isolate a derivative of strain B-3996 which no longer contained the plasmid pVIC40. The strain formed was streptomycin-sensitive and was designated B-3996kur. The method described by Hamilton et al., Journal of Bacteriology (1989) 171: 4617-4622, which was based on the use of the plasmid pMAK705 with a temperature-sensitive replicon, was used for incorporation of a deletion into the tdh gene which encodes threonine dehydrogenase. The plasmid pDR121 contained a DNA fragment from Escherichia coli 3.7 kilo-base pairs (kbp) in size, on which the tdh gene was coded. To generate a deletion of the tdh gene region, pDR121 was cleaved with the restriction enzymes ClaI and EcoRV and the DNA fragment 5 kbp in size isolated was ligated, after treatment with Klenow enzyme. The ligation batch was transformed in the E.coli strain DH5alpha and plasmid-carrying cells were selected. Successful deletion of the tdh gene was demonstrated after plasmid DNA isolation and control cleavage with EcoRI. The EcoRI fragment 1.7 kbp in size was isolated, and ligated with the plasmid pMAK705. The ligation batch was transformed in DH5alpha and plasmid-carrying cells were selected. The pMAK705 derivative formed was designated pDM32. For the gene replacement, B-3996kur was transformed with the plasmid pDM32. The replacement of the chromosomal tdh gene with the plasmid-coded deletion construct was carried out and was verified by standard PCR methods. The strain formed was tested for kanamycin sensitivity and was designated B-3996kurDELTAtdh. B-3996kurDELTAtdh was transformed with the plasmid pVIC40 isolated from B-3996 and plasmid-carrying cells were selected. A selected individual colony was designated B-3996kurDELTAtdh/pVIC40 and transformed with the plasmid pMW218mgo. Selection was carried out on LB-agar to which 20 microg/ml streptomycin and 50 microg/ml kanamycin were added. The strain formed in

this way was designated B-3996kurDELTAtdh/pVIC40, pMW218mqo. The preparation of L-threonine by the strains B-3996kurDELTAtdh/pVIC40 and B-3996kurDELTAtdh/pVIC40, pMW218mqo was tested, the minimal medium and the production medium not being supplemented with L-isoleucine. The minimal medium, the pre-culture medium and the production medium were supplemented with 20 microg/ml streptomycin for B-3996kurDELTAtdh/pVIC40 and with 20 microg/ml streptomycin and 50 microg/ml kanamycin for B-3996kurDELTAtdh/pVIC40, pMW218mqo. Results showed that B-3996kurDELTAtdh/pVIC40 and B-3996kurDELTAtdh/pVIC40, pMW218mqo produced 6.26 and 7.72 g/l of L-threonine, respectively. (39 pages)

L6 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2002:589786 CAPLUS
TITLE: Influence of threonine exporters on threonine production in Escherichia coli
AUTHOR(S): Kruse, D.; Kramer, R.; Eggeling, L.; Rieping, M.; Pfefferle, W.; Tchieu, J. H.; Chung, Y. J.; Saier, M. H., Jr.; Burkovski, A.
CORPORATE SOURCE: Degussa., R and D Feed Additives/Biotechnology, Halle,
33788, Germany
SOURCE: Applied Microbiology and Biotechnology (2002), 59(2-3), 205-210
CODEN: AMBIDG; ISSN: 0175-7598
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Threonine prodn. in Escherichia coli threonine producer strains is enhanced by overexpression of the E. coli **rhtB** and **rhtC** genes or by heterologous overexpression of the gene encoding the Corynebacterium glutamicum threonine excretion carrier, **thrE**. Both E. coli genes give rise to a threonine-resistant phenotype when overexpressed, and they decrease the accumulation of radioactive metabolites derived from [¹⁴C] L-threonine. The evidence presented supports the conclusion that both **RhtB** and **RhtC** catalyze efflux of L-threonine and other structurally related neutral amino acids, but that the specificities of these two carriers differ substantially.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L6 ANSWER 6 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:568125 BIOSIS
DOCUMENT NUMBER: PREV200100568125
TITLE: DNA coding for protein which confers on bacterium escherichia coli resistance to L-homoserine and method for producing L-amino acids.
AUTHOR(S): Livshits, VItaly Arkadievich (1); Zakataeva, Natalya Pavlovna; Aleoshin, Vladimir Venyamiovich; Balareova, Alla Valentinovna; Tokhmakova, Irina Lvovna
CORPORATE SOURCE: (1) Moscow Russia
ASSIGNEE: Ajinomoto Co., Inc., Tokyo, Japan
PATENT INFORMATION: US 6303348 October 16, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 16, 2001) Vol. 1251, No. 3, pp. No
Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

AB A bacterium which has an ability to produce an amino acid and in which a novel gene (**rhtB**) coding for a protein having an activity of making a bacterium having the protein L-homoserine-resistant is enhanced, is cultivated in a culture medium to produce and accumulate the amino acid

in the medium, and the amino acid is recovered from the medium.

L6 ANSWER 7 OF 16 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-05527 BIOTECHDS

TITLE: Fermentative production of L-threonine, useful in animal nutrition, comprises culturing enterobacterium with

increased

thrE gene activity;

Escherichia coli fermentation containing deleted tdh gene and Corynebacterium glutamicum mutant thrE gene

AUTHOR: RIEPING M

PATENT ASSIGNEE: DEGUSSA AG

PATENT INFO: DE 10102823 29 Nov 2001

APPLICATION INFO: DE 2000-1002823 27 May 2000

PRIORITY INFO: DE 2000-1026494 27 May 2000

DOCUMENT TYPE: Patent

LANGUAGE: German

OTHER SOURCE: WPI: 2002-115532 [16]

AB DERWENT ABSTRACT: NOVELTY - Fermentative production of L-threonine (I) using an Enterobacterium, especially one that already produces (I), in which activity of the thrE gene sequence (or sequences) is increased, particularly by overexpression, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) plasmid pZ1thrE containing the thrE gene of Corynebacterium glutamicum ATCC 13032; and (2) Brevibacterium flavum DM368-2 pZ1thrE, deposited as DSM 12840. BIOTECHNOLOGY - Preferred bacterium: This is of the family Enterobacteriaceae, preferably the genera Escherichia or Serratia, particularly E. coli. Other gene activities may also be increased, especially: (i) the ABC operon (aspartate kinase, homoserine dehydrogenase, homoserine kinase and threonine synthase); (ii) pyc (pyruvate carboxylase); (iii) pps (phosphoenolpyruvate synthase); (iv) ppc (phosphoenolpyruvate carboxylase); (v) pntA and pntB (transhydrogenases); (vi) gdhA (glutamate dehydrogenase); and (vi) rhtB (homoserine resistance). Optionally metabolic pathways that reduce formation of (I) are at least partially 'switched off'.

Preferably

the bacteria are transformed with a plasmid vector, specifically

pZ1thrE,

but activity may also be increased by e.g. using mutant regulatory elements, increasing half-life of mRNA and inhibiting decomposition of enzymes. Preferred process: Expression of thrE is induced, particularly with isopropyl beta-D-thiogalactopyranoside, and cells are cultured for 10-160 hr at preferably 30-40 degrees Centigrade. Preferred nucleic

acid:

The specification includes sequences of 2817 and 1909 bp for the thrE genes of Corynebacterium glutamicum ATCC 14752 and 13032, respectively, also of the deduced proteins sequences (both 489 amino acids).

Preparation: C. glutamicum ATCC 14752DELTAilvA was subjected to mutagenesis with transposon Tn5531 and mutants selected for retarded growth on medium containing threonylthreonyl-threonine (Thr3). One

mutant

that had the same growth as the parent strain in medium without Thr3 was identified and the insertion site in it was cloned and sequenced to identify a 1467 bp open reading frame for the thrE gene. The thrE gene from ATCC 13032 was isolated by polymerase chain reaction (primer sequences reproduced) and cloned conventionally into plasmids for subsequent cell transformation. USE - (I) is useful in animal nutrition, human medicine and the pharmaceutical industry. ADVANTAGE - Overexpression of thrE results in increased production of (I). EXAMPLE - The L-threonine-producing strain Escherichia coli B-3996 (US 5175107)

was

modified to delete the tdh gene, then transformed with pVIC40 (for resistance to streptomycin) and pMW218thrE (containing the Corynebacterium glutamicum thrE and kanamycin resistance genes). The transformants produced threonine at 7.57 g/l, compared with 6.26 g/l for a similar strain lacking pMW218thrE. (23 pages)

ACCESSION NUMBER: 2000:259844 CAPLUS

DOCUMENT NUMBER: 132:276602

TITLE: The **rhtB** gene conferring resistance to
L-homoserine to bacteria and its use in developing
strains for fermentation of amino acids

INVENTOR(S): Livshits, Vitaly Arkadievich; Zakataeva, Natalya
Pavlovna; Aleoshin, Vladimir Venyamiovich; Belareova,
Alla Valentinovna; Tokhmakova, Irina Lvovna

PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan

SOURCE: Eur. Pat. Appl., 14 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 994190	A2	20000419	EP 1999-118581	19990920
EP 994190	A3	20020814		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

RU 2144564	C1	20000120	RU 1998-118425	19981013
AU 9947550	A1	20000420	AU 1999-47550	19990913
US 6303348	B1	20011016	US 1999-396357	19990915
ZA 9906042	A	20000404	ZA 1999-6042	19990921
BR 9904955	A	20001212	BR 1999-4955	19991011
JP 2000116390	A2	20000425	JP 1999-289777	19991012
KR 2000029006	A	20000525	KR 1999-44027	19991012
CN 1254014	A	20000524	CN 1999-121353	19991013
US 2002102670	A1	20020801	US 2001-847392	20010503
US 2002058314	A1	20020516	US 2001-927395	20010813

PRIORITY APPLN. INFO.:

RU 1998-118425 A 19981013

US 1999-396357 A1 19990915

AB Amino acid-fermenting strains of *Escherichia coli* carrying an allele of the **rhtB** gene that makes them resistant to L-homoserine are described. The gene was identified and cloned using a mini-Mu phagemid with clones selected for by conferring homoserine resistance. Two genes conferring resistance were identified. One was the prior art **rhtA** gene and the other was the novel **rhtB** gene. The gene also confers resistance to a no. of other toxic amino acid analogs including .alpha.-amino-.beta.-hydroxyvaleric acid.

ACCESSION NUMBER: 2000:456755 CAPLUS

DOCUMENT NUMBER: 133:85119

TITLE: Production of L-amino acids by bacterium transformed
with amino acid excretion protein homologs

INVENTOR(S): Livshits, Vitaliy Arkadievich; Zakataeva, Natalia
Pavlovna; Nakanishi, Kazuo; Aleshin, Vladimir
Veniaminovich; Troshin, Petr Vladimirovich;
Tokhmakova, Irina Lvovna

PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan

SOURCE: Eur. Pat. Appl., 29 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1016710	A2	20000705	EP 1999-125263	19991217
EP 1016710	A3	20000906		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

RU 2175351		20011027	RU 1999-104431	19990309
AU 9964493	A1	20000706	AU 1999-64493	19991213
ZA 9907767	A	20000630	ZA 1999-7767	19991220
JP 2000189180	A2	20000711	JP 1999-373651	19991228
BR 9906287	A	20010123	BR 1999-6287	19991228
KR 2000048465	A	20000725	KR 1999-64627	19991229
CN 1261626	A	20000802	CN 1999-127522	19991230

PRIORITY APPLN. INFO.:

RU 1998-124016	A	19981230
RU 1999-104431	A	19990309

AB A bacterium belonging to the genus *Escherichia* is provided having an ability to produce an L-amino acid, wherein the ability to produce the L-amino acid is increased by increasing an expression amt. of an L-amino acid excretion protein. Thus, genes *yahN*, *yfiK*, *yeaS*, and *yggA* are isolated by PCR amplification and shown to have homol. with lysine transporter *LysE* of *Corynebacterium glutamicum* and *RhtB* protein. When these genes are amplified in *E. coli*, the transformed organism shows increased levels of L-amino acid prodn.

L6 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:441462 CAPLUS

DOCUMENT NUMBER: 133:69834

TITLE: Recombinant *Escherichia coli* strains containing genes *rhtC* and *rhtB* (encode proteins resulting in enhanced L-threonine and L-homoserine resistance activity) and use of strains for enhanced amino acid production

INVENTOR(S): Livshits, Vitaliy Arkadyevich; Zakataeva, Natalia Pavlovna; Aleshin, Vladimir Veniaminovich; Belareva, Alla Valentinova; Tokhmakova, Irina Lyvovna

PATENT ASSIGNEE(S): Ajinomoto Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 24 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1013765	A1	20000628	EP 1999-125406	19991220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
RU 2148642	C1	20000510	RU 1998-123511	19981223
JP 2000189177	A2	20000711	JP 1999-356018	19991215
AU 9965435	A1	20000629	AU 1999-65435	19991222
ZA 9907819	A	20000630	ZA 1999-7819	19991222
KR 2000048340	A	20000725	KR 1999-60483	19991222
CN 1260393	A	20000719	CN 1999-126909	19991223
BR 9906283	A	20010403	BR 1999-6283	19991223

PRIORITY APPLN. INFO.:

RU 1998-123511	A	19981223
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AB The invention provides recombinant *Escherichia coli* strains with enhanced L-threonine and L-homoserine resistance activity and use of these recombinant *E. coli* to increased prodn. of amino acids, including L-threonine, L-homoserine, L-valine and L-leucine. The invention also relates that the recombinant *E. coli* are produced by genetic transformation of genes *rhtC* and *rhtB*, encoding proteins resulting in enhanced L-threonine and L-homoserine resistance activity, resp. The invention further provides the: (1) DNA (gene *rhtC*) encoding the protein resulting in enhanced L-threonine; (2) DNA sequence of gene *rhtC*; (3) a primer and probe specific for the *rhtC* gene and (4) protein sequence of the proteins encoded by genes *rhtC* and *rhtB*. The invention also included the DNA sequence for gene *rhtB*. In the example section, the invention included: (1) cloning and identification

of

E. coli genes *rhtC* and *rhtB*; (2) methods used in prodn. of the recombinant E. coli strains and (3) effects of genes *rhtC* and *rhtB* proteins on homoserine and threonine prodn. in recombinant E. coli. The invention also reported on the homol. between the E. coli gene *rhtC* and *rhtB* proteins with lysine transporter *LysE* of *Corynebacterium glutamicum*.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L6 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:231966 CAPLUS

DOCUMENT NUMBER: 130:317177

TITLE: The formation enthalpies of rare earth-4d transition metal alloys and intermetallic compounds

AUTHOR(S): Ouyang, Yi Fang; Jin, Zhan Peng; Liao, Shu Zhi; Zhang,

Bang Wei

CORPORATE SOURCE: Dep. Phys., Guangxi Univ., Nanning, 530004, Peop. Rep.

China

SOURCE: Zeitschrift fuer Metallkunde (1999), 90(3), 242-244
CODEN: ZEMTAE; ISSN: 0044-3093

PUBLISHER: Carl Hanser Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The formation enthalpies of the title compds. were calcd. with Miedema's semiempirical method. The calcd. formation enthalpies are in good agreement with exptl. enthalpy data available.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L6 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3

ACCESSION NUMBER: 1999:424937 CAPLUS

DOCUMENT NUMBER: 131:196761

TITLE: The novel transmembrane *Escherichia coli* proteins involved in the amino acid efflux

AUTHOR(S): Zakataeva, Natalia P.; Aleshin, Vladimir V.; Tokmakova, Irina L.; Troshin, Petr V.; Livshits, Vitaliy A.

CORPORATE SOURCE: Ajinomoto-Genetika Research Institute, Moscow, Russia

SOURCE: FEBS Letters (1999), 452(3), 228-232

CODEN: FEBLAL; ISSN: 0014-5793

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A novel gene of *E. coli*, *rhtB*, was characterized. Amplification of this gene provides resistance to homoserine and homoserine lactone. Another *E. coli* gene, *rhtC*, provides resistance to threonine. The homologs of *RhtB* are widely distributed among various eubacteria and archaea; 1-12 copies of family members that differ in their primary structure were found in the genomes. Most of them are genes that encode hypothetical transmembrane proteins. Exptl. data that indicate participation of the *rhtB* product in the excretion of homoserine were obtained.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L6 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4

ACCESSION NUMBER: 1999:514310 CAPLUS

DOCUMENT NUMBER: 131:296676

TITLE: A new family of amino-acid-efflux proteins

AUTHOR(S): Aleshin, Vladimir V.; Zakataeva, Natalia P.;
Livshits,
Vitaliy A.
CORPORATE SOURCE: State Research Institute of Genetics and Selection of
Industrial Microorganisms, Moscow, 113545, Russia
SOURCE: Trends in Biochemical Sciences (1999), 24(4), 133-135
CODEN: TBSCDB; ISSN: 0376-5067
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Multiple alignment of **RhtB** proteins is reported. The authors
have found a set of proteins that are homologous to **RhtB** in a
wide range of prokaryotes that includes proteobacteria, cyanobacteria,
bacilli, mycobacteria, and the archaea *Archaeoglobus fulgidus* and
Methanobacterium thermoautotrophicum. The authors suggest that
RhtB is involved in the efflux of homoserine and threonine in *E.*
coli. It is proposed that the **RhtB** proteins belong to a new,
widespread class of functionally important transporters that allow
excretion of metabolites from different prokaryotes and archaea.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR
THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L6 ANSWER 14 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1997:419723 BIOSIS
DOCUMENT NUMBER: PREV199799718926
TITLE: Characterization of a pleiotropic mutation that confers
upon *Escherichia coli* cells resistance to high
concentrations of homoserine and threonine.
AUTHOR(S): Zakataeva, N. P.; Aleoshin, V. A.; Livshits, V. A.
CORPORATE SOURCE: State Inst. Genetics Selection of Industrial
Microorganisms, Moscow Russia
SOURCE: FASEB Journal, (1997) Vol. 11, No. 9, pp. A935.
Meeting Info.: 17th International Congress of Biochemistry
and Molecular Biology in conjunction with the Annual
Meeting of the American Society for Biochemistry and
Molecular Biology San Francisco, California, USA August
24-29, 1997
ISSN: 0892-6638.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

L6 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:739143 CAPLUS
DOCUMENT NUMBER: 126:63530
TITLE: Hydriding characteristics of terbium and rhodium
intermetallics
AUTHOR(S): Kulshreshtha, S. K.; Jayakumar, O. D.
CORPORATE SOURCE: Chem. Div., Bhabha At. Res. Cent., Bombay, 400 085,
India
SOURCE: Journal of Materials Science Letters (1996), 15(22),
1942-1944
CODEN: JMSLD5; ISSN: 0261-8028
PUBLISHER: Chapman & Hall
DOCUMENT TYPE: Journal
LANGUAGE: English

AB TbrRh2 started to absorb H after the second activation cycle and attained
a

satn. compn. of TbrRh2H3.0 in the fourth cycle of hydration. The crystal
structure of TbrRh2H3.0 was too complex to index by x-ray diffraction
patterns. TbrRh needed three cycles of activation, and the satn. compn.
was TbrRh2.7. The crystal structure of TbrRh2.7 could be indexed as
orthorhombic with $a = 0.3872$, $b = 1.1368$, and $c = 0.4606$ nm which
corresponds to a lattice dilation of .apprx.27%.

ACCESSION NUMBER: 1995:569194 CAPLUS

DOCUMENT NUMBER: 123:15351

TITLE: Standard enthalpies of formation of terbium alloys, Tb+Me (Me .ident. Ni, Ru, Rh, Pd, Ir, Pt), by high-temperature direct synthesis calorimetry

AUTHOR(S): Guo, Qiti; Kleppa, O. J.

CORPORATE SOURCE: The James Franck Institute, The University of Chicago,

5640 South Ellis Avenue, Chicago, IL, 60637, USA
SOURCE: Journal of Alloys and Compounds (1995), 221(1-2), 50-5

CODEN: JALCEU; ISSN: 0925-8388

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The std. enthalpies of formation of 12 Tb alloys with late transition metals were detd. by direct synthesis calorimetry at 1474. \pm .2 K. The values were TbNi5 -(27.4. \pm .0.9), TbRu2 -(23.6. \pm .1.7), Tb5Ru2 -(29.9. \pm .1.9), TbRh -(72.3. \pm .1.1), TbRh2 -(64.4. \pm .1.5), TbPd -(85.2. \pm .1.6), Tb3Pd4 -(85.5. \pm .1.4), TbPd3 -(78.8. \pm .1.5), TbIr2 -(70.6. \pm .2.6), TbPt -(115.7. \pm .2.9), TbPt2 -(96.7. \pm .3.1), and TbPt3 -(85.6. \pm .2.9) kJ/g-atom. The results are compared with predicted values from the A.R. Miedema model (1983) and with available literature data for TbPd and TbPt.